(11)

Eosinophils and inflammation

In inflamed tissues, eosinophils have been shown to be capable of antagonizing and inactivating histamine and other chemical mediators of inflammation, such as 5-HT and bradykinin. Through this function, the eosinophil helps to limit and circumscribe the inflammatory process.

The eosinophilic response to an inflammatory stimulus is characterized by accumulation of eosinophils in the inflamed tissues, with a simultaneous increase both in the production of eosinophils by the bone marrow and in the number of circulating eosinophils (eosinophilia), on their way from the bone marrow to the inflammatory sites. Chronic eosinophilia occurs in response to complex antigens, as in helminthic (worm) infestations (e.g. hook-worm, ascaris and bilharzia) and in response to allografts (e.g. skin grafts).

The accumulation of eosinophils in inflammatory sites may be inhibited by high doses of corticosteroids, which also depress the chemotactic attraction of eosinophils.

12)

Eosinophilia

From the foregoing account we may deduce that eosinophilia occurs in pathological states as a result of an antigen—antibody reaction.

Common causes of eosinophilia include:

1 Parasitic disease, e.g. worm infestations of the gut.

2 Allergic conditions:

(a) Bronchial asthma.

(b) Allergic rhinitis (hay fever).

(c) Drug reactions, e.g. penicillin sensitivity.

3 Tropical eosinophilia, which represents a reaction to the filaria parasite.

4 Dermatological diseases.

Functions of basophils

The distinguishing morphological feature of the basophil is the large blue-black granules which appear to fill the cytoplasm, overlie the nucleus and tend to obscure nuclear configuration. Basophil granules contain abundant acid mucopolysaccharide, which accounts for their strong affinity for basic dyes such as methylene blue. Heparin is one of the important acid mucopolysaccharide constituents; other constituents include histamine, 5-HT and ribonucleic acid (RNA). The basophil is the carrier of histamine in the blood and, due to its being rich in both heparin and histamine, it bears a strong resemblance to tissue mast cells. The function of basophils is not known with certainty but they may have a role related to their content of the physiologically active substances, such as heparin, histamine and 5-HT. Mast cells and basophils have surface Igt receptors which bind IgE coated antigens, degranulate and release histamine leading to allergic reactions e.g. urticaria.

Monocytes (blood macrophages)

This macrophage has its origin in the bone marrow monoblast and promonocyte. The mature monocyte reaches the bloodstream, where it stays for a variable period of time, ranging from a few hours to 6 days. Then it leaves the circulation for the tissues, where it undergoes transformation to the larger and more effective phagocyte—tissue macrophage (histiocyte).

Functions

The macrophage contributes directly to the body defence systems by phagocytosis and killing of invading bacteria and, indirectly, by interacting and cooperating with lymphoid cells in both the afferent (or recognition of foreign material) and efferent (effector) limbs of the immune response. In the afferent limb, macrophages process the antigen and present it to lymphocytes.

Macrophages phagocytose damaged or altered host cells and microscopic debris, which justifies the descriptive name '**tissue scavengers**'.

Lymphocytes

Much of our knowledge about the cellular elements of the blood has been based on the concept that cells may be recognized and classified by morphological criteria. This concept, however, does not hold in relation to recognizing and classifying cells of the lymphoid series. The blood lymphocytes constitute a family of cells of different origins, migration patterns, sizes, staining characteristics, ultrastructure, lifespan and function.

Formation (lymphopoiesis)

Lymphocytes originate from the primitive unipotent stem cell (lymphoid-committed precursor) in the **thymus, lymphoid tissues** and **bone marrow** and then proceed along a known maturation line via the 'lymphocyte production pathway', which includes the following cellular stages:

1 *Lymphoblasts*. Normally these are only seen in lymphopoietic organs and almost never observed in peripheral blood.

2 *Intermediate (transitional) forms* (large blast cells).

3 *Small and large lymphocytes* (blood lymphocytes).

These stages are not unidirectional. The process can, under certain circumstances, go in the reverse direction and small lymphocytes can grow into large lymphocytes and lymphoblasts. Such blastic transformation can be demonstrated *in vitro* by growing small lymphocytes in a suitable culture medium containing a non-specific mitogen, such as *phytohaemagglutinin (PHA)*, or a specific antigen, e.g. *tuberculin*.

Lymphocytes in the bloodstream

Lymphocytes enter the peripheral blood either directly, by passing through the walls of blood-vessels in the various lymphopoietic organs, or indirectly, by entering the lymph stream and eventually reaching the bloodstream through the thoracic duct and other lymph ducts in the neck.

Classification

When seen under an ordinary light microscope, blood lymphocytes can be divided into **small** (5–8 μm diameter) and **large lymphocytes** (8–15 μm diameter). The majority of blood lymphocytes are of the small type.

Functions

Lymphocytes are the central cells in immunity. On the basis of this function, lymphocytes are divided into two types:

1 *Thymus-dependent lymphocytes (T cells)* are so called because they originate in the thymus or bone marrow and migrate to the thymus where they mature and are reprogrammed to recognize foreign antigens. They have a lifespan of 100–300 days or even more (hence the name long-lived lymphocytes). This long lifespan is closely related to their property of constant movement from blood to tissues to lymph to blood again (*recirculation of lymphocytes*).

T lymphocytes are the principal mediators of **cellular immune responses**, such as rejection of tissue graft, e.g. kidney transplant, and delayed hypersensitivity reactions. They also play a minor role in the synthesis of immunoglobulins (antibodies).

2 *Thymus-independent lymphocytes (B cells)*. In humans, the B cells develop in the bone marrow, the germinal centres of lymph nodes and the red pulp of the spleen. Their lifespan is 2–7 days (hence the name short-lived lymphocytes). They have been called B cells because they are known as bursa cells. When the B cells are properly stimulated by an antigen, they develop successively into large lymphocytes and, lastly, plasma cells. The plasma cells are lymphoid cells which are capable of producing **antibodies**. Thus, the B lymphocytes are the principal mediators of the **humoral immune response**.

Total leucocyte count

Although it is usually quoted in textbooks that the total leucocyte count is 4000 to 10 000 cells per cubic millimetre of blood, it should be emphasized that this range applies more to Europeans than to residents of hot tropical countries. It is not uncommon to find a total leucocyte count among healthy students and blood donors in these geographical locations of between 2000 and 4000 cells/mm^3. Because there is a relatively low count of neutrophils, this is called *neutropenia.*

Differential white cell counts

The normal proportions of white blood cells are as follows:

Neutrophils	60–70%
Lymphocytes	20–30%
Monocytes	2–8%
Eosinophils	2–4%
Basophils	0–2%

Leucocytosis and leucopenia

An increase in the total leucocyte count above the normal is called leucocytosis. This may occur in health (physiological leucocytosis) or disease.

Physiological leucocytosis may occur under several conditions:

1 Diurnal variation: leucocyte counts are lowest in the morning and increase to a maximum in the afternoon.
2 After a protein meal.
3 Following physical exercise.
4 Stimulation by stress or an injection of adrenaline (epinephrine).

Disease states which commonly cause leucocytosis are bacterial infections (pyogenic infections), e.g. tonsillitis, infected wounds or inflamed appendix. In these conditions, measurement of the total leucocyte count is essential for diagnosing the existence of the infection. The differential white cell count is also useful. In general, acute bacterial infections cause an increase in the neutrophil count, while chronic and viral infections are associated with an increased lymphocyte count.

Leucopenia is a decrease in the total leucocyte count below the normal. It is often seen in conditions of malnutrition and is also an important feature of typhoid fever. Some drugs may depress the bone marrow and therefore result in leucopenia and, in particular, a decrease in the granulocyte count (agranulocytosis). Leucopenia can also be caused by a deficiency of vitamin B_{12} or folic acid.

Table 19.2	Significance of High and Low White Blood Cell Counts	
WBC Type	**High Count May Indicate**	**Low Count May Indicate**
Neutrophils	Bacterial infection, burns, stress, inflammation.	Radiation exposure, drug toxicity, vitamin B_{12} deficiency, and systemic lupus erythematosus (SLE).
Lymphocytes	Viral infections, some leukemias.	Prolonged illness, immunosuppression, and treatment with cortisol.
Monocytes	Viral or fungal infections, tuberculosis, some leukemias, other chronic diseases.	Bone marrow suppression, treatment with cortisol.
Eosinophils	Allergic reactions, parasitic infections, autoimmune diseases.	Drug toxicity, stress.
Basophils	Allergic reactions, leukemias, cancers, hypothyroidism.	Pregnancy, ovulation, stress, and hyperthyroidism.

Types of Leukemia.

Leukemias are divided into two general types:

1- lymphocytic leukemias.
2. myelocytic leukemias.

* The leukemia cells are bizarre & undifferentiated & not identical with any of the normal white blood cells.

* Usually the more undifferentiated the cells the more acute is the leukemia.

* But with some of the more undifferentiated cells, the process can be quite chronic, sometimes developing slowly over a period of 10-20 years.

* Leukemic cells, especially the very undifferentiated cells, are usually nonfunctional.

Effects of Leukemia on the Body:

1. The first effect of leukemia is metastatic growth of leukemic cells in abnormal areas of the body.

2. The leukemic cells of the bone marrow invade the surrounding bone.

3. Almost all leukemias spread to the spleen, the lymph nodes, the liver & vascular regions.

4. In each of these areas the rapidly growing cells invade the surrounding tissues, utilizing the metabolic elements of these tissues & consequently casing tissue destruction.

5. Very common effects in leukemia are the development of infections, severe anemia & bleeding tendency caused by thrombocytopenia (lack of platelets).

6. The most important effect of leukeima on the body is the excessive use of metabolic substrates by the growing cancerous cells.

7. Tremendous demands are made on the body for foodstuffs, especially the amino acids & vitamins. Consequently, the energy of the patient is greatly depleted, rapid deterioration of the normal protein tissues of the body.

8. Obviously, after metabolic starvation has continues long enough, this alone is sufficient to cause death.